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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,147	02/19/2004	Richard E. Weller	23-65308	5344

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	PAPER NUMBER
1618	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,147	WELLER ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 26-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 February 2004 and 19 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/28/04,4/3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Claims 1-35 are pending in the application.

2. Claims 1-18 and 26-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups I,II,IV and V, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/26/07.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what units are intended for the average molecular weight of the polypeptide block as the units are absent.

5. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what constitutes a "substantial amount" or "substantially spherical" in regards to the 90-yttrium phosphate particles. The specification does not provide adequate guidance for one skilled in the art to utilize the invention commensurate in scope with the instant claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leavitt et al. (US 5,942,209) in view of Kanapilly et al. (*Int. J. Radiat. Isot.* **1971**, *22*, 567-575) and Horowitz et al. (US 5,368,736)) and further in view of Churchill et al. (US 4,942,035).

8. Leavitt et al. (US 5,942,209) discloses a polymer hydrogel composition capable of delivering radioactive agents, such as yttrium-90 microspheres (column 4, line 17; column 7, lines 6-7) to a local site of a disease for treatment (column 2, lines 18-20). The hydrogel formulation, with yttrium-90 incorporated therein, may be prepared to allow for controlled release and may be selected to degrade at a known rate under conditions encountered at the site of application (column 1, lines 53-56). The advantage of such a delivery vehicle is that by altering the radionuclide the duration and intensity of the radionuclide exposure from the polymeric matrix can be adjusted (column 2, lines 20-24). The hydrogel is formed from a biodegradable polymer, such as Pluronic F-68 (polyethylene glycol block copolymer) which is complexed to polylysine, polyglutamic acid polymers via peptide linkages (column 2, lines 39-59; column 3, lines 42-43). The radionuclide may be chelated to a polymer, such as a protein or a nucleic acid (column 4, lines 48-52; column 6, lines 24-31). Leavitt et al. does not disclose the use of 90-

yttrium phosphate or polypeptides with an average molecular weight from about 300-30,000.

9. Horowitz et al. (US 5,368,736) discloses that the separation of curie quantities and purification of 90-yttrium as the phosphate from the parent nuclide, 90-strontium (column 2, lines 13-19) is possible via the method of Kanapilly et al. Yttrium-90 has been used for the treatment of cancer and rheumatoid arthritis of the knee joint (column 1, lines 14-17) and is an attractive radionuclide for therapeutic applications (column 1, lines 35-36). Curie quantities of radionuclide are necessary for therapeutic applications. The development of site-specific methods for treating various forms of cancer via radiolabled conjugates requires curie quantities of pure yttrium-90. Yttrium-90 must be essentially free of 90-strontium as it is known to cause bone marrow suppression and could also interfere with the radiolabeling process and compete for binding sites on the conjugate. The method of Kanapilly et al. is disclosed as providing for such purified 90-yttrium conjugates.

10. Kanapilly et al. (*Int. J. Radiat. Isot.* **1971**, *22*, 567-575) discloses the method of separating and purifying curie quantities of 90-yttrium phosphate as colloidal suspensions (p568, paragraphs 2 and 3; p569, paragraph 1; p574, conclusion).

11. Churchill et al. (US 4,942,035) discloses a pharmaceutically acceptable copolymer hydrogel (column 2, lines 39-42) containing a polypeptide hydrophilic polymer of minimum average molecular weight of 5,000 (column 5, line 35) and a hydrophobic polymer, such as polyethylene glycol (column 3, lines 25-43; column 4, line 25).

12. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the 90-yttrium phosphate of Horowitz et al. (Kanapilly et al.) into the hydrogel composition of Leavitt et al. In order for a radiotherapeutic treatment to be successful an ample supply of the radionuclide needs to be accessible. The generation of curie quantities of 90-yttrium phosphate via the method of Kanapilly allows for such quantities to be created. The purified form ensures that the therapeutic amount of radiation delivered to a target/diseased site will be precisely that which is desired for treatment.

13. The hydrogel of Leavitt et al. is interchangeable with the hydrogel of Churchill et al. as they both are polypeptide-polymeric compositions that form gels in aqueous solution and are capable of delivering a therapeutic agent to a subject and thus one would have been motivated to use a polypeptide hydrophilic polymer with a minimum average molecular weight of 5,000 with a reasonable expectation of success.

14. Claims 19,20 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leavitt et al. (US 5,942,209) in view of Kanapilly et al. (*Int. J. Radiat. Isot.* **1971**, *22*, 567-575 as disclosed in Horowitz et al. (US 5,368,736)) and further in view of Kimura et al. (US 5,415,851) and Davis et al. (*J. Nucl. Med.* **1989**, *30*, 1047-1055).

15. Leavitt et al. (US 5,942,209) discloses a polymer hydrogel composition capable of delivering radioactive agents, such as yttrium -90 microspheres (column 4, line 17;

column 7, lines 6-7) to a local site of a disease for treatment as well as that stated above.

16. Horowitz et al. (US 5,368,736) discloses that the separation of curie quantities and purification of 90-Y as the phosphate from the parent nuclide, 90-Sr (column 2, lines 13-19) is possible via the method of Kanapilly et al. as well as that stated above.

17. Kanapilly et al. (*Int. J. Radiat. Isot.* **1971**, *22*, 567-575) discloses the method of separating and purifying curie quantities of 90-yttrium phosphate as colloidal suspensions (p568, paragraphs 2 and 3; p569, paragraph 1; p574, conclusion).

18. Kimura et al. (US 5,415,851) discloses the preparation of spherical particles of rare earth phosphate phosphors containing yttrium and that the light-emitting efficiency of the rare earth-based phosphors is high when the particles are as close to spherical as possible and have a particle diameter in the range of 0.01 to 1μm (column 1, lines 23-32 and 58+; column 2, line 4). The method from preparing the spherical rare earth phosphate phosphors, such as yttrium allows for precipitation/purification without agglomeration of fine primary particles (column 2, lines 25-28 and 32).

19. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the colloidal 90-yttrium phosphate of Horowitz et al. (Kanapilly et al.) into the hydrogel composition of Leavitt et al. In order for a radiotherapeutic treatment to be successful an ample supply of the radionuclide needs to be accessible. The generation of curie quantities of 90-yttrium phosphate via the method of Kanapilly allows for such quantities to be created. The purified form ensures that the therapeutic amount of radiation delivered to a target/diseased site will be precisely that which is desired for

treatment. It would have been obvious to use the spherical 90-yttrium phosphate particles of Kimura et al. to provide for the greatest light-emitting efficiency of the beta particles of yttrium for the treatment of diseased tissue in a subject and allows for diagnostic imaging via scintigraphy.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 19-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14 and 21-25 of U.S. Patent No. 7,087,244 in view of the combined disclosures of Leavitt et al. (US 5,942,209) and Kanapilly et al. (*Int. J. Radiat. Isot.* **1971**, *22*, 567-575) as disclosed in Horowitz et al. (US 5,368,736)). The thermogelling, biodegradable polymer composition of 7,087,244

encompasses the therapeutic carrier of the instant claims. The therapeutic carrier of the instant claims and the thermogelling, biodegradable polymer composition of 7,087,244 comprise a biocompatible polymer block (polyethylene glycol) and a polypeptide block with a molecular weight from about 300-30,000. The combined disclosures Leavitt et al. of Horowitz et al. describe a polymer composition comprising a polyethylene glycol block-polypeptide block with a 90-yttrium phosphate therapeutic agent. The 90-yttrium phosphate therapeutic agent anticipated the bioactive agent of 7,087,244.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
April 3, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER